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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/730,209	12/08/2003	Amy L. Rubinstein	26007.0003U2	4631

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NEEDLE & ROSENBERG, P.C.  
SUITE 1000  
999 PEACHTREE STREET  
ATLANTA, GA 30309-3915

EXAMINER
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BERTOGLIO, VALARIE E

ART UNIT	PAPER NUMBER
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1632

MAIL DATE	DELIVERY MODE
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12/20/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	10/730,209		RUBINSTEIN ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Valarie Bertoglio		1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☐ Responsive to communication(s) filed on 08/16/2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 1-5 and 16-35 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 15 is/are allowed.
- 6) ☒ Claim(s) 11-14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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### **DETAILED ACTION**

Applicant's amendment filed 08/16/2007 has been received. Claim 11 has been amended. Claims 6-10 are cancelled. Claims 1-5 and 11-35 are pending. Claims 1-5 and 16-35 are withdrawn. Claims 11-15 are under consideration in the instant office action.

#### ***Sequence Non-Compliance***

Applicant has amended the specification to appropriately include Sequence Identification Numbers. The application is now sequence compliant.

#### ***Claim Rejections - 35 USC § 112, 1<sup>st</sup> Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 11-14 under 35 U.S.C. 112, first paragraph, as lacking enablement for the full breadth of the claims is withdrawn in light of Applicant's amendments to the claims.

#### ***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 11-15 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11 and 12 remain rejected under 35 U.S.C. 102(b) as being anticipated by Motoike et al (Genesis 28:75-81, 2000; of record in IDS). The rejection is maintained for reasons of record set forth at pages 11-12 of the office action dated 02/12/2007.

Applicant's arguments have been fully considered and are not persuasive.

Applicant argues that Motoike fails to disclose, expressly or inherently, comparison between Tie2-GFP mutant and wildtype fish to identify the mutant gene as involved in blood vessel growth. In response, Motoike teaches at pages 77-78, that the reporter line (Tie2-GFP) can be crossed to mutant lines to investigate morphological changes in the vasculature to study vascular development. Such an investigation would inherently involve a comparison using wildtype Tie2-GFP fish as a control or baseline for comparison. One would necessarily compare with a wild-type fish, or the results would have no meaning. One of ordinary skill in the art would understand that the property of comparing to a wild-type fish is inherent in a method step of studying development (growth) of a mutant fish as it is standard methodology in the art that determining a difference in morphology in a mutant requires comparison to a wildtype control. Thus, the recited comparison step of the claims is inherent in the teachings of Motoike. Additionally, differences in blood vessel development between the wildtype and mutant fish would be an indicator of altered blood vessel growth, as claimed. Thus, while Motoike does not expressly teach each and every aspect of the limitations of the claims, the limitations are inherent to the teachings.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 13 and 14 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Motoike et al. as applied to claims 11 and 12 above, and further in view of Matz et al (Nature 17:969-973, 1999; of record in IDS). The rejection is maintained for reasons of record set forth at pages 12-14 of the office action dated 02/12/2007.

As disclosed above, Motoike et al teaches a transgenic zebrafish comprising a GFP reporter gene operably linked to the Tie2 promoter. Motoike et al do not specifically teach a green reef coral fluorescent protein or a red fluorescent protein.

However, Matz et al teaches clones of six fluorescent proteins homologous to green fluorescent protein isolated from reef corals. They further disclose two of these have spectral characteristics different from GFP, emitting at yellow and red wavelengths. They are disclosed that they were used for *in vivo* labeling in mammalian cell culture and mRNA injection of frog embryos (abstract).

Therefore, at the time of filing it would have been obvious to make a transgenic zebrafish as taught by Motoike et al expressing a coral reef GFP or red fluorescence protein as taught by Matz et al. One would be motivated to use the coral reef GFP or red fluorescence protein because it would be useful in *in vivo* labeling experiments as taught by Matz et al. One would have a reasonable expectation of success because making GFP transgenic zebrafish was established in the art and the CGFPs are homologous and were used in *in vivo* labeling experiments in frog eggs and mammalian cells.

Applicant's arguments have been fully considered and are not persuasive.

Applicant argues that simply because Motoike discloses that the Tie2-GFP fish (zebrafish) can be used to visualize vascular development does not mean that any changes in blood vessels resulting from an altered blood vessel gene could be assessed in a fish resulting from a cross between a Tie2-GFP fish and a mutant fish. In response, Motoike expressly teaches such a cross (page 78, col.1, lines 1-2). Applicant argues that just because blood vessels can be visualized, it does not mean that any changes in growth caused by a mutant gene could also be observed in order to identify a blood vessel related gene that is involved in blood vessel growth. In response, this argument is not fully clear to the Examiner. It is not apparent what is lacking in Motoike that would not enable one of skill in the art to determine a mutant gene as having a role in blood vessel growth. Presence of a vessel, visualized by reporter expression, in a wildtype fish that is not present in the corresponding mutant fish would indicate that the mutant gene has a role in the growth of the absent vessel. Applicant is recommended to clarify this argument by pointing out that which is lacking in the teachings of Motoike other than expressly reciting a comparison step, which is inherent given the knowledge on the ordinary skilled artisan (see above).

Applicant argues that until the present invention, there was no evidence that changes in a blood vessel related gene would result in changes in blood vessel growth (para bridging pages 13-14). Applicant argues that those in the art would not expect that identification of blood vessel related genes involved in blood vessel growth would be possible.

In response, at the time of filing, there were known mutants with defects in genes that alter blood vessel growth. Notably, Childs et al (Feb 2002, Development, 129:973-982; IDS) taught the *obd* mutant that display abnormal blood vessel growth. Childs used the mutant, by comparison to wildtype, to demonstrate a difference in vessel growth as a result of the gene defect. Other mutants, such as *gridlock*, were also known in the art (Weinstein *et al*, Nature Medicine, 1995, (IDS) 1:1143-1147; Roman *et al*, Development, 129:3009-3019).

### ***Conclusion***

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Claim 15 is free of the art.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Valarie Bertoglio, Ph.D./

Primary Examiner

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